

CLAIMS

1. A method of preparing a porphyrin derivative starting from a meso-substituted porphyrin compound, **characterized** in that a meso-(2'-cyanovinyl)-substituted porphyrin compound of which the vinyl is optionally substituted is used as the meso-substituted porphyrin compound, wherein said meso-(2'-cyanovinyl)-substituted porphyrin compound, in a form in which its porphyrin macrocycle is complexed with a bivalent metal ion

i) is subjected to

an acid for which  $0 < \text{pKa} < 5$

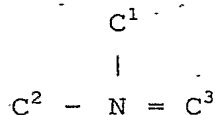
and

an oxidising agent,

with the restriction that if the carbon atom of the porphyrin macrocycle at which the (2'-cyanovinyl) substituent is attached is designated  $\text{C}\alpha$ , there must be a substituent attached to  $\text{C}\delta$ , counting along the perimeter of the porphyrin macrocycle, said substituent comprising a -C-C motif directly attached at the  $\text{C}\delta$  carbon atom;

or

ii) is subjected under aprotic conditions to a Vilsmeier reagent having a reactive motif



containing a quaternary nitrogen atom which is directly linked to two carbon atoms  $\text{C}^1$ ,  $\text{C}^2$  wherein said carbon atoms are not part of a unsaturated or aromatic moiety, and which quaternary nitrogen atom is directly linked to a carbon atom  $\text{C}^3$  via a double bond, said carbon atom  $\text{C}^3$  carrying a halogen atom chosen from fluoro, chloro, bromo and iodo

with the restriction that if the carbon atom of the porphyrin macrocycle at which the (2'-cyanovinyl) substituent is attached is designated  $\text{C}\alpha$ , there must be a sub-

stituent attached to C $\delta$ , counting along the perimeter of the porphyrin macrocycle, said substituent comprising a -CH motif directly attached at the C $\delta$  carbon atom;

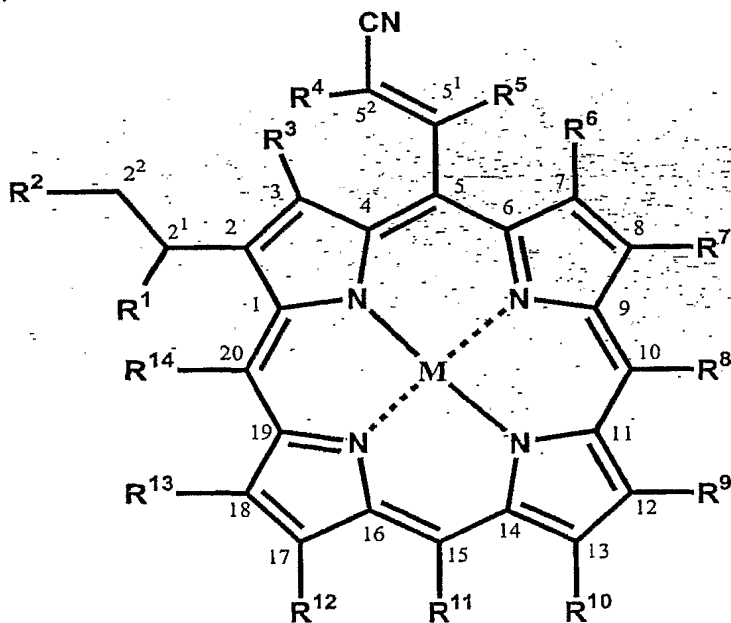
to convert said meso-(2'-cyanovinyl)-substituted porphyrin

- 5 compound into a porphyrin derivative having a quinoline-ring system peri-condensed to the porphyrin ring, and optionally the bivalent metal ion is removed or replaced by another metal ion, and optionally the nitrogen atom of the quinoline-ring system ring is quaternized.

- 10 2. The method according to claim 1, **characterized** in that for alternative step i) a meso-(2'-cyanovinyl)-substituted porphyrin compound of formula (I) is used as the starting compound,

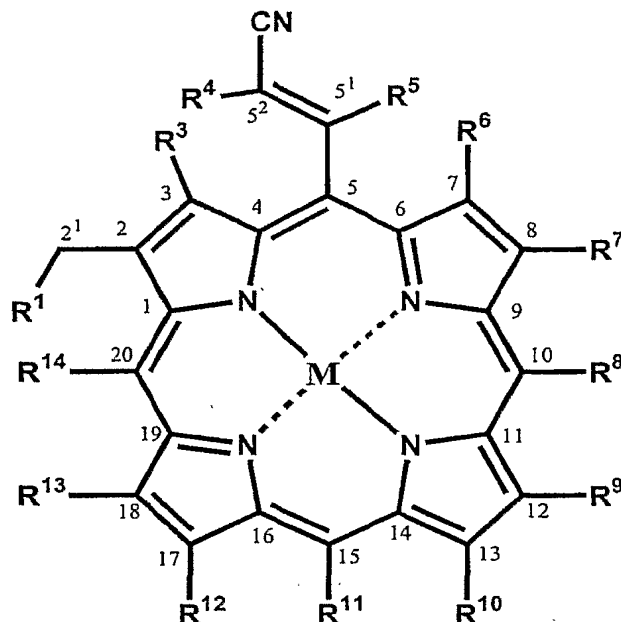
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(I)



- or wherein for alternative step ii) meso-(2'-cyanovinyl)-substituted porphyrin compound of formula (III) is used as the starting compound
- 20

(III)



wherein

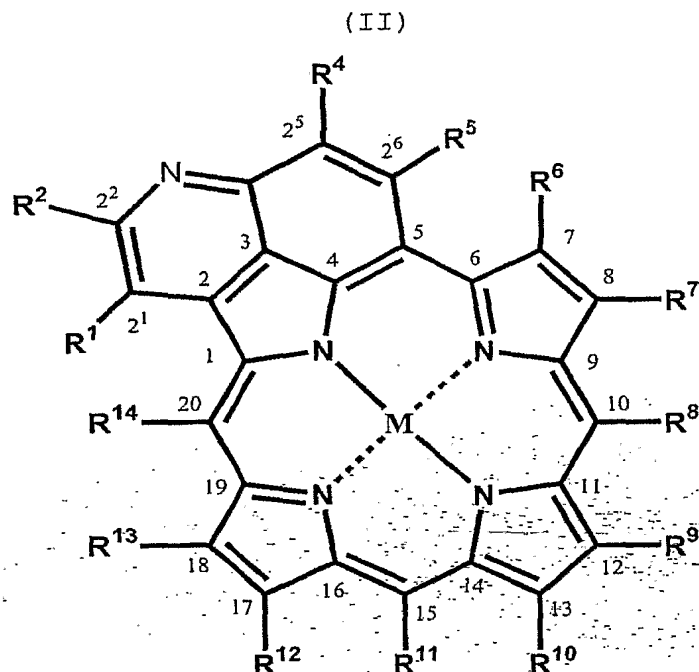
- 5        R<sup>1</sup>, R<sup>2</sup> represent independently of each other hydrogen, linear or branched (C<sub>1-8</sub>) alkyl, or linear or branched (C<sub>1-8</sub>) alkyl C(O)O (C<sub>1-8</sub>) alkyl, wherein the groups comprising alkyl may optionally be substituted with fluoro, chloro, bromo, iodo, nitrile, (C<sub>1-8</sub>) thioether, and (C<sub>1-8</sub>) alkoxy;
- 10        R<sup>3</sup> represents H or (C<sub>1-8</sub>) alkyl;
- R<sup>4</sup> and R<sup>5</sup>, represent, independently of each other, hydrogen, nitrile, monocyclic, bicyclic or tricyclic (C<sub>6-14</sub>) aryl, or (C<sub>1-4</sub>) alkyl wherein the aryl and alkyl group may optionally be substituted with fluoro, chloro, bromo, iodo, nitrile, (C<sub>1-8</sub>) thioether, and (C<sub>1-8</sub>) alkoxy;
- 15        R<sup>6</sup> to R<sup>14</sup> represent independently of each other, hydrogen, linear or branched (C<sub>1-8</sub>) alkyl, linear or branched (C<sub>1-8</sub>) alkyl C(O)O (C<sub>1-8</sub>) alkyl, wherein n is an integer of 0 to 4, CH<sub>2</sub>=CH-, a monocyclic, bicyclic or tricyclic (C<sub>3</sub>-C<sub>14</sub>) aryl, which aryl may optionally contain one or more nitrogen atoms as heteroatoms; and R<sup>8</sup>, R<sup>11</sup>, and R<sup>14</sup> may in addition represent an acrylonitrile group substituted with R<sup>4'</sup> and R<sup>5'</sup>, wherein
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$R^{4'}$  and  $R^{5'}$  are as defined for  $R^4$  and  $R^5$ ;

and

M represents a bivalent metal ion,  
 wherein the compound of formula (I) or (III) is converted  
 5 into the corresponding porphyrin derivative of formula (II)  
 comprising a quinoline-ring system fused to the porphyrin  
 ring



10 wherein the substituents have the meanings given  
 above, and depending on the meaning of  $R^8$ ,  $R^{11}$ , and  $R^{14}$  and the  
 correspondence of an adjacent  $R^7$ ,  $R^9$ ,  $R^{10}$ ,  $R^{12}$ , and  $R^{13}$  with  $R^3$   
 optionally more than one quinoline-ring system peri-condensed  
 15 to the porphyrin ring is present.

3. The method according to claim 1 or 2, **characterized**  
 in that the nitrogen atom of the peri-condensed quinoline-  
 ring system ring in formula (II) is quaternized.

4. The method according to any of the preceding claims,  
 20 **characterized** in that the meso-(2'-cyanovinyl)-substituted  
 porphyrin compound is prepared by introducing a formyl or  
 acetyl residue at a meso position of a porphyrin compound,  
 whereafter the mesoformylporphyrin thus formed is converted

into the meso-(2'-cyanovinyl) derivative.

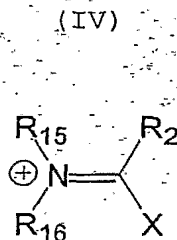
5. The method according to claim 4, **characterized** in that the mesoformylporphyrin formed is converted into the meso-(2'-cyanovinyl)-substituted porphyrin compound by reaction with diethylphosphonoacetonitril.

6. The method according to any of the preceding claims, **characterized** in that the porphyrin starting compound for the preparation of the meso-(2'-cyanovinyl) porphyrin is chosen from the group of i) hemin, and ii) heme.

7. The method according to any of the preceding claims, **characterized** in that  $\text{Ni}^{2+}$  is used as the bivalent metal ion.

8. The method according to any of the preceding claims, **characterized** in that a Brönsted-acid is used with the proviso that  $0 < \text{pK}_a < 5$ , the reaction being carried out at a temperature above  $140^\circ\text{C}$ .

9. The method according to any of the claims 1 to 7, **characterized** in that the Vilsmeier reagent used is of the formula (IV)



wherein

R15 and R16 are, independently of each other, linear or branched  $\text{C}_{1-8}$  alkyl,

X is fluoro, chloro, bromo and iodo, and

R2 is hydrogen, linear or branched  $(\text{C}_{1-8})$  alkyl, or linear or branched  $(\text{C}_{1-8})$  alkyl  $\text{C}(\text{O})\text{O}$   $(\text{C}_{1-8})$  alkyl, wherein the groups comprising alkyl may optionally be substituted with fluoro, chloro, bromo, iodo, nitrile,  $(\text{C}_{1-8})$  thioether, and  $(\text{C}_{1-8})$  alkoxy.

10. The method according to claim 9, **characterized** in that X is chloro or bromo.

11. Porphyrin derivatives, wherein said derivatives are:

- 2'-methoxycarbonylquino[4,4a,5,6-jkl]-annulated 12-demethyl-13-de[2-(methoxycarbonyl)ethyl]mesoporphyrin dimethylester;
- 2'-methoxycarbonylquino[4,4a,5,6-qrs]-annulated 18-demethyl-17-de[2-(methoxycarbonyl)ethyl]mesoporphyrin dimethylester;
- quino[4,4a,5,6-abt]-annulated 2-demethyl-3-deethylmesoporphyrin dimethylester;
- quino[4,4a,5,6-efg]-annulated 7-demethyl-8-deethylmesoporphyrin;
- 2'-methoxycarbonylquino[4,4a,5,6-jkl]-annulated 12-demethyl-13-de[2-(methoxycarbonyl)ethyl]mesoporphyrin;
- 2'-methoxycarbonylquino[4,4a,5,6-qrs]-annulated 18-demethyl-17-de[2-(methoxycarbonyl)ethyl]mesoporphyrin;
- quino[4,4a,5,6-abt]-annulated 2-demethyl-3-deethylmesoporphyrin;
- quino[4,4a,5,6-bcd]-2-demethyl-3-deethyl-mesoporphyrin dimethylester;
- quino[4,4a,5,6-bcd]-2-demethyl-3-deethyl-mesoporphyrin;
- 3'-methylquino[4,4a,5,6-efg]-7-demethyl-8-deethylmesoporphyrin dimethylester;
- 3'-methylquino[4,4a,5,6-efg]-7-demethyl-8-deethylmesoporphyrin;
- 9'-aminocarbonylquino[4,4a,5,6-efg]-7-demethyl-8-deethylquinoporphyrin dimethylester;
- 9'-aminocarbonylquino[4,4a,5,6-efg]-7-demethyl-8-deethylquinoporphyrin
- N-benzylquinolinium[4,4a,5,6-efg]-annulated mesoporphyrin dimethylester
- N-benzylquinolinium[4,4a,5,6-efg]-annulated mesoporphyrin.

12. A porphyrin derivative having a quinoline-ring system peri-condensed to the porphyrin ring.

13. Use of a porphyrin derivative according to claim 12 for the preparation of a pharmaceutical composition of a porphyrin derivative according to the invention for prevention of and/or treating

1) benign, malignant, inflamed and infectious skin and mucosa disorders: skin/mucosa disorders;

2) vascular disorders;

3) tumors and pre-cancerous lesions;

5 4) ophthalmology disorders;

5) gynecological or urological disorders;

6) immunological disorders;

7) oral cavity or nasopharyngeal disorders.

14. Use of a porphyrin derivative according to claim 12  
10 for the preparation of a composition of a porphyrin derivative according to the invention for the preparation of a composition

1) for photodetection of malignant and pre-malignant lesions;

15 2) for decontamination or pathogen reduction of liquids such biological fluids and contaminated water;

3) for decontamination or pathogen reduction of surfaces;

4) for use as insecticide.

20 15. Pharmaceutical composition comprising a porphyrin derivative according to claim 12 together with a pharmaceutically acceptable carrier or excipient.